

383

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
5 October 2000 (05.10.2000)

PCT

(10) International Publication Number  
**WO 00/58514 A3**

(51) International Patent Classification<sup>7</sup>: C12Q 1/68 (74) Agent: LINKKILA, Timothy, P.; Testa, Hurwitz & Thibeault, LLP, High Street Tower, 125 High Street, Boston, MA 02110 (US).

(21) International Application Number: PCT/US00/07882

(22) International Filing Date: 24 March 2000 (24.03.2000) (81) Designated States (national): AU, CA, JP.

(25) Filing Language: English (84) Designated States (regional): European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

(26) Publication Language: English (30) Priority Data:  
09/277,016 26 March 1999 (26.03.1999) US Published: — with international search report

(71) Applicant: EXACT LABORATORIES, INC. [US/US]; (88) Date of publication of the international search report:  
63 Great Road, Maynard, MA 01754 (US). 13 December 2001

(72) Inventors: LAPIDUS, Stanley, N.; 12 Old Evergreen Road, Bedford, NH 03110 (US). SHUBER, Anthony, P.; 11 Grant Street, Milford, MA 01757 (US). *For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*



WO 00/58514 A3

BEST AVAILABLE COPY

(54) Title: METHODS FOR IMPROVING SENSITIVITY AND SPECIFICITY OF SCREENING ASSAYS

(57) Abstract: Methods of the invention comprise assays for markers indicative of cancer or precancer. Assays of the invention are performed on samples obtained from a patient by non-invasive or minimally-invasive methods. The invention provides nucleic acid indicia of cancer or precancer with high sensitivities and high specificities for detection.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/07882

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CHEM ABS Data, MEDLINE, BIOSIS, EMBASE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SIDRANSKY DAVID: "Nucleic acid-based methods for the detection of cancer." SCIENCE (WASHINGTON D C), vol. 278, no. 5340, 7 November 1997 (1997-11-07), pages 1054-1058, XP002170462 ISSN: 0036-8075 page 1054 -page 1057; table 1	1-8, 15-17, 20-24, 29-33
Y	WO 95 00669 A (PHARMACIA BIOTECH AB ;Baylor College Medicine (US); CASKEY C THOMA) 5 January 1995 (1995-01-05) page 14, line 1 - line 28; claims 1-18	9-14
Y	---	9-14
	---	-/-

*BEST AVAILABLE COPY*

Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority, claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*Z\* document member of the same patent family

Date of the actual completion of the international search

2 July 2001

Date of mailing of the international search report

17/07/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.  
Fax: (+31-70) 340-3016

Authorized officer

Gabriels, J

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 00/07882

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication where appropriate, of the relevant passages	Relevant to claim No.
X	VET JACQUELINE A M ET AL: "Comparative analysis of p53 mutations in bladder washings and histologic specimens." AMERICAN JOURNAL OF CLINICAL PATHOLOGY, vol. 110, no. 5, November 1998 (1998-11), pages 647-652, XP001009905 ISSN: 0002-9173 page 650, right-hand column -page 652, left-hand column ---	1,6,8, 16,17, 22-25,32
X	CAWKWELL L ET AL: "Frequency of allele loss of DCC, p53, RBI, WT1, NF1, NM23 and APC/MCC in colorectal cancer assayed by fluorescent multiplex polymerase chain reaction." BRITISH JOURNAL OF CANCER, vol. 70, no. 5, 1994, pages 813-818, XP001009897 ISSN: 0007-0920 page 817; figure 2 ---	1-6, 15-17, 22-24, 22,33
X	WO 96 29430 A (WAYNE JOHN CANCER INST ;NAT GENETICS INST (US)) 26 September 1996 (1996-09-26) claims 1-20 ---	1,8,16, 17, 22-24,32
X	DE 197 36 691 A (GIESING MICHAEL PROF DR MED) 25 February 1999 (1999-02-25) claims 1-4 ---	1-8, 15-17, 20-24, 32,33
A	HOANG JEAN-MARC ET AL: "BAT-26, an indicator of the replication error phenotype in colorectal cancers and cell lines." CANCER RESEARCH, vol. 57, no. 2, 1997, pages 300-303, XP002162454 ISSN: 0008-5472 page 300 -page 302 ---	18,19

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

PCT/US 00/07882

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9500669	A 05-01-1995	SE 501439 C AT 185843 T AU 698553 B AU 7212194 A DE 69421277 D DE 69421277 T EP 0705349 A EP 0969103 A ES 2141828 T JP 9501312 T SE 9302152 A US 6153379 A		13-02-1995 15-11-1999 29-10-1998 17-01-1995 25-11-1999 31-05-2000 10-04-1996 05-01-2000 01-04-2000 10-02-1997 23-12-1994 28-11-2000
WO 9629430	A 26-09-1996	AU 5310296 A EP 0871768 A US 6057105 A		08-10-1996 21-10-1998 02-05-2000
DE 19736691	A 25-02-1999	WO 9910528 A EP 1007740 A		04-03-1999 14-06-2000

**BEST AVAILABLE COPY**